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EXAMINER

SMITH, CAROLYN L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/901,782

Applicant(s)

HARDIN ET AL.

Examiner

Carolyn L. Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 10-19,25-34,48 and 49 is/are pending in the application.
- 4a) Of the above claim(s) 25-34 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10,11,17 and 18 is/are allowed.
- 6) ☒ Claim(s) 12-16,19,48 and 49 is/are rejected.
- 7) ☒ Claim(s) 12 is/are objected to.
- 8) ☒ Claim(s) 10-19,25-34,48 and 49 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 3/11/05, has been entered.

Cancelled claims 1-9, 20-24, and 35-47, amended claims 16, 19, withdrawn claims 25-34, and new claims 48-49, filed 3/11/05, are acknowledged.

Claims herein under examination are 10-19 and 48-49.

#### ***Claim Objections***

Claim 12 is objected to because of the following informality: Claim 12 (line 3) recites the phrase "the a" which does not make grammatical sense. Appropriate correction is requested.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-16, 19, and 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 12 (line 2) recites the phrase “the first conformational state” which lacks clear antecedent basis as there is no previous mention of this phrase in claim 12 or in claim 10 from which it depends. Claims 13-16 are also rejected due to their direct or indirect dependency from claim 12.

Claim 19 (line 2) recites the phrase “a site selected from the group consisting of 513-518, 643, 647, 649, and 653-661” which lacks clarity as to which type of site this is of the Taq polymerase. It is also unclear what the units are for the listed numbers. Clarification of these issues via clearer claim wording is requested.

Claim 48 (line 3) recites the phrase “the tags” which lacks clear antecedent basis. There is insufficient basis for this phrase as only a singular tag was previously mentioned. Clarification of this issue via clearer claim wording is requested. Claim 49 is also rejected due to its dependency from claim 48.

Claim 48 (penultimate line) lists numbers “513-518, 643, 647, 649 and 653-661” which lack clarity because the units for these numbers are not mentioned. Clarification of this issue via clearer claim wording is requested. Claim 49 is also rejected due to its dependency from claim 48.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (WO 0036151) in view of Brandis (Nucleic Acids Research, 1999 Vol. 27, No. 8), Voet et al., and *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594).

This rejection is necessitated by amendment.

Williams describes a *Taq* DNA polymerase (p. 8, lines 23-28) in which a fluorescently labeled dNTP (tag) is associated with the polymerase during monomer incorporation (p. 8, lines 1-9). Williams describes a fluorophore and quencher pair being incorporated into oligo probes (p. 2, lines 16-18). The dNTP tag consists of a labeled nucleotide triphosphate (NTP) having a  $\gamma$ -phosphate with a fluorophore moiety attached and a quencher moiety that sufficiently prevents fluorescence until incorporation of the NTP at which time the  $\gamma$ -phosphate with the fluorophore moiety is released and detected (p. 8, lines 10-20). As Webster's II New Riverside Dictionary defines a tag as a piece of something that identifies, classifies or labels; one reasonable interpretation of the quencher is a tag whose close presence to the fluorophore tag results in fluorescent signal disappearance (p. 2, lines 16-25). Williams describes the fluorescence is detected when labeled dNTPs are incorporated into the strand and fluorescence is induced (p. 9, lines 28-29). Williams describes that upon incorporation, the fluorescent dye molecule is released with pyrophosphate from the polymerase and then swept away from the parent DNA molecule by the flow (p. 10, lines 13-17), suggesting the polymerase's detectable property reverts back to its initial state. Williams describes that as the polymerase moves along the DNA, the nucleotide sequence is read from the order of released dyes (p. 14, lines 30-31). Williams describes the possible presence of other polymerases, such as HIV reverse transcriptase, as stated in instant claim 48. Williams describes acquiring a sequence of images/movies (read outs) of

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fluorophores in order to track the path of single dyes involved in monomer incorporation (page 8, first paragraph; page 12, third paragraph; page 13, second paragraph; page 14, fourth paragraph) as well as data storage units that record detection (page 15, second and third paragraph), continuously imaging at video rate in fluorescent and non-fluorescent forms (page 14, line 24 to page 15 line 7), and pixel samplings (page 15, last paragraph) which represent the first and second values, as stated in instant claim 49. Williams does not describe covalent bonding or the numerical amino acid binding sites.

Brandis describes a *Taq* DNA polymerase I including an inherent characteristic that polymerases go through conformational changes (abstract). Brandis also describes that a change occurs in a fluorescent label during the change in conformational states of the polymerase when nucleotide binding occurs as the polymerase is active (abstract). Voet et al. describe a transition state theory allowing the understanding of how enzymes catalyze reactions (p. 332, col. 2, first paragraph). Voet et al. describe a high-energy (unstable) complex existing with covalent bonds during a bimolecular reaction (p. 332, col. 2, second paragraph).

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to “prove that subject matter shown to be in the prior art does not possess characteristic relied on” (205 USPQ 594, second paragraph, first full paragraph).

As Williams, Brandis and Voet et al. describe a *Taq* DNA polymerase (p. 8, lines 23-28) in which a fluorescently labeled dNTP (tag) covalently bonded to the polymerase during

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monomer incorporation, a skilled artisan would have been motivated to believe this composition would inherently include the characteristics of having the tag covalently bonded to one of the amino acid sites listed in instant claim 48. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to realize identical compositions (i.e. the polymerizing agent, such as described by Williams and Brandis) and would have identical characteristics, as stated by *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594). Thus, Brandis (Nucleic Acids Research, 1999 Vol. 27, No. 8), Voet et al., and *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) motivate the limitations of instant claims 48 and 49.

### ***Conclusion***

Claims 10-11 and 17-18 are allowable.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 30, 2005

*Ardin H. Marschel 4/3/05*  
ARDIN H. MARSCHEL  
PATENT EXAMINER